REMARKS

Claims 21-36 are presently pending in the case. Though Applicant disagrees with the rejection of claim 32 and reserves the right to pursue the claim in a continuing application, claim 32 has been amended to expedite prosecution. Dependent claim 36 has been added. Support for the amendments can be found throughout the specification as originally filed.

Reconsideration of the present case in view of the remarks herein is requested.

Claim rejections under 35 USC 102(a)

The Examiner rejected claim 32 and 36 under 35 USC 102(a) as being anticipated by European Patent Application EP 0 808 635 to Howlett (hereinafter "Howlett"). The rejection is traversed.

Howlett does not anticipate claim 32. Claim 32 is to a device for controlling the delivery of an aerosolized active agent comprising a flow resistance modulator that initially provides a first flow resistance and that subsequently provides a second flow resistance, the second flow resistance being less than the first flow resistance. In contrast, Howlett discloses a device where its initial flow resistance (as shown by the configuration shown in Figure 2) is the minimum flow resistance, and as a patient generates more pressure, the flow resistance increases. The flow resistance is never lower than it is in the initial configuration. Thus, Howlett does not disclose a flow resistance modulator that provides a second flow resistance that is less than the initial flow resistance. Accordingly, Howlett does not anticipate claim 32.

The Examiner's contention that the Howlett device may, in some circumstances, have a second flow resistance that is less than another resistance does not make Howlett an anticipatory reference. The Examiner states that if "a patient's initial inhalation (negative) pressure exceeds the threshold of the flow resistance modulator AND any subsequent inhalation (negative) pressure is both below the threshold of the flow resistance modulator and below the initial inhalation pressure, then it is reasonable to conclude that the second flow resistance ... is less than the first flow resistance." Applicant disagrees with the characterization. First, the concept that a patient can generate an initial inhalation pressure that would exceed the threshold is not based in reality. A user is not capable of generating such an instantaneous vacuum.

Secondly, even if such a situation could be achieved, it would not meet the limitations of claim 32. Claim 32 recites an initial flow resistance, not an initial inhalation pressure. The initial configuration of the Howlett device is as shown in Figure 2 of the reference. It would then, under the Examiner's hypothetical, have to move from the configuration shown in Figure 2 to a more restrictive configuration after the user generates the threshold exceeding pressure. Thus, the configuration shown in Figure 2 is the initial configuration and provides the initial flow resistance, and Howlett cannot have a second flow resistance that is less than this initial flow resistance.

Claims 33-36 depend from claim 32 and are allowable over Howlett for at least the same reasons as the claim from which they depend.

Claim rejections under 35 USC 103(a)

The Examiner rejected claims 21-31 under 35 USC 103(a) as being unpatentable over Howlett. The rejection is traversed.

Howlett does not render Applicant's invention as set forth in claim 21 unpatentable because it does not teach or suggest all features positively recited in the claim. Claim 21 is to a device for controlling the delivery of an aerosolized active agent to the lungs comprising, inter alia, a flow resistance modulator that provides a high flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM. Howlett does not disclose or suggest a flow resistance modulator that provides a high flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM. Therefore, all elements of claim 21 are not taught or suggested by the reference.

Additionally, it would not have been obvious to one of ordinary skill in the art to modify the Howlett device in such a way as to arrive at the invention set forth in claim 21. For example, Howlett teaches away from modifying the device so that it provides a high flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM. Instead, Howlett teaches the desirability of controlling the flow rate at 30 to 60 liters per minute (column 3 lines 43-50). One of ordinary skill in the art would readily recognize that a user of the device would find it difficult (if not impossible) to generate sufficient inhalation pressures to sustain a flow in the desired range taught by Howlett, if the Howlett device were modified to have a high flow resistance as claimed. Thus, it would not have been obvious to provide Howlett's device with a high flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM, in view of the specific teachings of Howlett.

A simplified analysis of the flow further illustrates the non-obviousness of the Examiner's proposed modification to the Howlett device. The flow rate is related to the pressure drop and the flow resistance by the relationship $Q = P^{1/2} / R$, where Q is the flow rate, P is the pressure drop, and R is the flow resistance. Rearranging this formula to solve for pressure gives $P = (RQ)^2$. If the flow resistance R is 0.4 (cm H_2O)$^{1/2}$ / SLM, for a flow rate of 30 to 60 SLM, the necessary pressure drop that a user would have to generate would be 144 to 576 cm H_2O. Generating these pressures (including those on the lower end) would be very uncomfortable for even a healthy patient, and would be virtually impossible for a diseased patient. As discussed in the Clark et al. 1993 Journal of Aerosol Medicine article entitled "The Relationship Between Powder Inhaler Resistance and Peak Inspiratory Conditions in Healthy Volunteers- Implications for In Vitro Testing" (previously submitted), the peak inspiratory pressure drop for healthy individuals is on average around 80 cm H_2O and the comfortable inspiratory pressure drop is about 30-35 cm H_2O (see pages 104 and 105). Thus, one of ordinary skill in the art would be motivated to provide a flow resistance that would allow the user to pull 30 to 60 liters per minute through the device, and would have been taught away from providing a flow resistance of at least 0.4 (cm H_2O)$^{1/2}$ / SLM. Accordingly, it would not have been obvious to the person of ordinary skill to modify Howlett as proposed by the Examiner.

Furthermore, Applicant disagrees with the Examiner's suggestion that "mere routine experimentation and observation" would arrive at the claimed flow resistance. Contrary to the Examiner's contention, if a person of ordinary skill in the art were to perform the suggested routine experimentation and observation, it would be with the objective of providing the Howlett-taught flow rate of 30 to 60 liters per minute. As discussed above, the flow resistance recited in claim 21 would not result from such experimentation and observation. Thus, there is no motivation to modify the Howlett device as suggested by the Examiner, aside from Applicant's own disclosure, which the person of ordinary skill in the art would not have had the benefit of reading. Therefore, the Examiner is using impermissible hindsight reasoning in suggesting that Applicant's invention of claim 21 is rendered obvious by the reference. When considering the teachings of Howlett as a whole, the person of ordinary skill would not be motivated to modify Howlett to arrive at Applicant's invention of claim 21.

By including a flow resistance modulator that provides a high flow resistance of at least 0.4 (cm H_2O)$^{1/2}$ / SLM, Applicant's invention has several advantages over prior art devices, such as Howlett. For example, as discussed in Applicant's specification, the high flow resistance

may be used during at least a portion of the delivery process to provide an active agent to a patient in a manner that increases the bioavailability of the agent. This unexpected advantage resulting from the high flow resistance is further evidence of the non-obviousness of the feature.

Claims 22-27 depend from and include the limitations of claim 21. Therefore, Howlett does not render claims 22-27 unpatentable for at least the reasons discussed above. In addition, claim 24, for example, further recites that the high flow resistance corresponds to a flow rate of 15 liters per minute or less. Since Howlett teaches a flow rate of 30-60 liters per minute, it does not teach or suggest a flow resistance corresponding to a flow rate of 15 liters per minute or less.

Howlett also does not render independent claim 28 unpatentable. Claim 28 is to a device for controlling the delivery of an aerosolized active agent to the lungs of a human comprising a flow resistance modulator that provides a high flow resistance which corresponds to a flow rate of about 15 liters per minute or less and subsequently provides a lower flow resistance. Howlett specifically teaches the desirability of controlling the flow at a rate of 30 to 60 liters per minute. Therefore, Howlett does not disclose or suggest the invention of claim 28 and does not render the claim unpatentable. Applicant disagrees with the Examiner's contention on page 5 of the Office Action of December 5, 2001 that a reduction in flow resistance caused merely by patient relaxation renders claim 28 unpatentable. Howlett's flow controller controls inlet orifice size to maintain the flow rate through the device at 30 to 60 liters per minute. Therefore, when the flow rate is below 30 liters per minute, the inlet orifice size would be at a maximum (i.e. the flow resistance is a minimum). According to the invention as set forth in claim 28, the flow restrictor must be able to provide a lower flow resistance than the flow resistance that is provided at a flow rate of 15 liters per minute. Since the flow resistance in Howlett is at a minimum when the flow rate is 15 liters per minute, the flow resistance cannot be modulated to a lower flow resistance.

In addition, it would not have been obvious to one of ordinary skill in the art to modify Howlett to arrive at the invention of claim 28. Specifically, Applicant also disagrees with the Examiner's conclusion that one of ordinary skill in the art would find it obvious to increase flow resistance in order to allow the device to be used by patients with less than average breathing capacity. First, there is no mention in Howlett that the device is designed solely for healthy patients. Secondly, if one of ordinary skill in the art were to be so inclined to modify the Howlett device in accordance with the Examiner's suggestions, the artisan would decrease

Howlett's flow resistance rather than increase Howlett's flow resistance. Thus, the Examiner has not provided motivation for making the proposed modification.

The Examiner's statement that Howlett discloses a flow resistance modulator "which is fully capable of providing the recited function of exerting resistances to flow of at least 0.4 (cm H20)1/2/SLM" is not supported by the reference. Note that even at its maximum flow resistance, air is still allowed to flow through the inlets (reference numeral 31) of Howlett. Note, too, that the air flow is controlled to be at 30 to 60 liters per minute (column 3 line 47). As discussed above, a flow resistance of at least 0.4 (cm H20)1/2/SLM would not allow for the air flow to be controlled at 30 to 60 liters per minute. Therefore, Applicant contends that the Examiner has mischaracterized the reference. The Examiner is requested to point to a specific teaching in Howlett that supports the Examiner's contention.

For at least the reasons above, the invention set forth in claim 28 is not rendered obvious by the teachings of Howlett nor are claims 29-31 which depend from claim 28. Accordingly, it is requested that the rejections be withdrawn.

Information Disclosure Statement

Applicant has filed a number of information disclosure statement in compliance with MPEP section 609. For example, information disclosure statements were filed on July 28, 2000, on February 26, 2001, on April 3, 2001, on August 31, 2001, on September 20, 2001, on March 5, 2002, and on October 29, 2002. Applicant included in a previous response copies of the statements and copies of the postcard returned by the Patent Office indicating that the information disclosure statements were received. Applicant request indication of the consideration of the references cited in the information disclosure statements.

Conclusion

The claims are allowable for the reasons given above. Thus, the Examiner is respectfully requested to reconsider the present rejections and allow the presently pending claims. Should the Examiner have any questions, the Examiner is requested to call the undersigned at the number given below.

Respectfully submitted,

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Dated: November 21 , 2002

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